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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,132	09/14/2005	Stephen Strittmatter	23380-602 Natl	7561

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EXAMINER	
DUTT, ADITI	

ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
07/16/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/519,132	STRITTMATTER ET AL.	
	Examiner	Art Unit	
	Aditi Dutt	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *3-6 and 9-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,7 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-17* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 December 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/23/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

1. The amendment of 24 May 2007 has been entered in full. Claims 1-17 are pending in the instant application.

Election with traverse

2. Applicant's election with traverse of Group I, claims 1, 7 and 8, in the reply filed on May 24, 2007 is acknowledged.

3. The traversal is on the ground(s) that the inventions of Groups I-V, although may be independent or distinct, would not appear to place an undue search burden on the Examiner, because the inventions of Groups I-V, would significantly overlap with each other. This is found persuasive in part because claim 2, of Group II, is broadly interpreted by examiner to read upon binding of a RGM to a Neogenin protein, the scope of which overlaps with the invention of Group I. Claims 2, 7 and 8 of Group II are rejoined and will be examined in the instant application. However, Applicant's arguments are not found persuasive with regards to rejoining of Groups III, IV and V. Although Groups III, IV and V recite a method for monitoring the interaction between RGM and a Neogenin, they involve special technical features that are not required by each of the other methods (previous Office Action, page 3). The special technical features

are as follows: Group III comprises the binding of a fusion protein comprising a RGM domain with cells expressing a Neogenin ; Group IV comprises co-culturing embryonic nerve cells with cells transfected with an expression construct encoding the RGM and which express the Neogenin; Group V comprises culturing embryonic nerve cells under conditions to display growth cones.

This requirement is still deemed proper and is therefore made FINAL.

4. Applicant timely traversed the restriction (election) requirement in the reply filed on May 24 2007.

5. Claims 1, 2, 7 and 8, drawn to a method for identifying an agent which modulates the binding of an RGM (repulsive guidance molecule) to a neogenin, comprising detecting and monitoring the binding, are being considered for examination in the instant application.

Sequence Compliance

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. Specifically, the sequences disclosed in Figures 5 and 6A and 6B, are not accompanied by the required reference to the relevant SEQ ID

NO. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825).

Appropriate correction is required.

Drawings

7. Figures 5, 6A and 6B, are objected to because tables and sequence listings that are included in the specification are, except for applications filed under 35 U.S.C. 371, not permitted to be included in the drawings (see 37 CFR 1.83(a) and 1.58(a); MPEP § 608.02). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement

Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

8. Claims 1, 2, 7 and 8 are objected to because of the following informalities:

Claims 1 and 2 are objected to because of the following informalities: Acronym "RGM" recited should be spelled out in all independent claims for clarity.

Claims 7 and 8 are objected to because they depend from non-elected claims 3, 4, 5 and 6.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1, 7 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. The term "modulating" in claim 1 is a relative term which renders the claim indefinite. The term "modulating" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear what the term "modulating" encompasses. Is it "inhibiting", "activating" or "mimicking"?

11. The term "monitoring" in claim 2 is unclear, as it is not ascertainable as to whether the term monitoring means observing and recording the observations (e.g. binding data) over a period of time, OR is it merely detecting the binding?

12. Claims 1 and 2 are also rejected because of the limitation reciting "a Neogenin", which is interpreted as "any" Neogenin. It is not clear whether this encompasses more than one "Neogenin" type (e.g. splice variants etc.).

13. Claims 7 and 8 are rejected as they depend from rejected claims 1 and 2.

Claim Rejections - 35 USC § 112-Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 1, 2, 7 and 8, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method

for identifying an agent which modulates the binding of RGMa or RGMb to a Neogenin, and a method for determining the specific binding of RGMa/RGMb to Neogenin, does not reasonably provide enablement for the identification of an agent that modulates the binding of any RGM to Neogenin, and a method for monitoring the binding of any RGM to Neogenin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

15. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, include the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

16. The claims are drawn to a method for identifying an agent which modulates the binding of any RGM to a Neogenin, comprising incubating a mixture of an isolated mammalian (human) RGM and an isolated mammalian (human) Neogenin in the presence of an agent, and detecting the specific binding between RGM and Neogenin, wherein a difference in the binding, in the presence or absence of the agent, will indicate that the agent modulates the binding. It is to be noted that the term "a RGM" is

broadly interpreted as encompassing any RGM subtype. Additionally the term "modulates" is interpreted as encompassing "activates" or "inhibits" (see instant specification, page 15, para 3).

17. The specification of the instant application teaches that RGM is a 33/35 kDa molecule that is active during vertebrate nervous system development (page 2, para 2; page 14, para 2). The specification also identifies Neogenin, having a sequence homology with the Netrin receptor, Deleted in colorectal cancer (DCC), as a specific receptor for RGM (page 5, para 2-3). Still further, the specification teaches that the mouse genome has 3 RGM related sequences, mRGM-A, mRGM-B and mRGM-C, sharing a 41-49% identity with each other, RGM-A sharing a 80% identity with chick or cRGM. Furthermore, RGM-A and RGM-B are expressed in various regions of the developing mouse brain and bind to the neogenin receptor (page 12, para 2; Figure 1E). The specification further teaches that both RGM and neogenin are highly expressed in the adult nervous system as well as in the injured nervous system, thus implying a role in the adult neural regeneration (page 14, para 2). The specification finally demonstrates RGM binding sites in the brain by expressing a fusion protein comprising RGM-A fused to human placental alkaline phosphatase (AP) in HEK293 cells (page 12, para 1). However, the specification does not teach any methods or working examples to indicate that all RGM molecules will bind to Neogenin, and further to identify an agent that will

modulate the binding of all RGM molecules to Neogenin. Undue experimentation would be required of a skilled artisan to determine such.

18. Relevant literature teaches that RGM, a membrane bound glycosylphosphatidylinositol (GPI)-anchored glycoprotein, is an axon guidance molecule consisting of 3 homologs in vertebrates, RGMa, RGMb and RGMc, with RGMa and RGMb showing abundant expression in the early stages of development of the mouse CNS (Yamashita et al. Curr Opin Neurobiol 17: 29-34, 2007; pages 29-30). The art also teaches that RGMa is expressed in the hippocampus and dentate gyrus of mice, whereas RGMc is expressed in the skeletal muscle (Matsunaga et al. Dev Gr Diff 46: 481-486, 2004; page 482, col 1, para 2). Matsunaga et al further teach that RGMa knockout mice reveal defects in neural tube closure; RGMb is involved in cell adhesion of dorsal root ganglia neurons, while RGMc is involved in iron metabolism (page 483, para 1). The art further teaches that RGM binds to a Netrin binding protein, Neogenin, with a higher affinity than that exhibited by Netrin (Yamashita et al. page 30), the RGM-neogenin interaction resulting in axon repulsion (Rajagopalan et al. Nat Cell Biol 6: 756-762, 2004, page 761, last para). As observed from the instant specification and the relevant art, although, both RGMa and RGMb, bind to neogenin, RGMa is more extensively studied. On the other hand, neither the instant specification, nor the relevant literature provides any information on the binding characteristics of RGMc to neogenin. Hence, the state of prior and post art do not enable a method to monitor

the binding of any RGM to neogenin or a method to identify an agent which modulates the binding of any RGM to neogenin. In the absence of guidance regarding the binding of all RGM molecules to Neogenin and the effectiveness of identifying an agent that will modulate the binding of these molecules with a reasonable amount of success, undue experimentation would be required of a skilled artisan. The specification must provide such guidance commensurate in scope with the claims.

19. Due to the large quantity of experimentation necessary to identify an agent which modulates the binding of any RGM molecule to neogenin, and monitor such binding, the lack of direction/guidance presented in the specification; the absence of working examples directed to same; the complex nature of the invention; the unpredictability of the binding of all RGM molecules with neogenin; and the breadth of the claims which fail to recite specific RGM molecules, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Conclusion

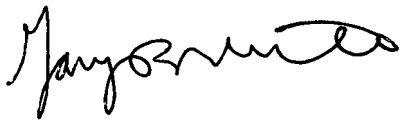
20. No claims are allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aditi Dutt whose telephone number is (571) 272-9037. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:00 p.m.

22. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

23. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov/. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AD
29 June 2007



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